CASE REPORTS

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Cardiac Pacing for Cardiac Arrest Due to Hyperkalemia plus Digitalis and Quinidine Toxicity

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LIFE-THREATENING HYPERKALEMIA may develop suddenly in cases of potassium overdosage or gradually in a variety of kidney disorders, and may remain undetected until a preterminal state has been reached. It is not widely known that cardiac pacing can be employed successfully in this emergency. Recent reviews of artificial pacing[1,2] and treatment of potassium intoxication[3,4] fail to mention cardiac pacing in managing severe hyperkalemia. Indeed, this therapeutic method has been reported in only four patients to date.[5,6] Cardiac pacing for atrioventricular block and asystole caused by digitalis toxicity has been recommended[7,8] but reports of such are rare.[9] The same is true of quinidine poisoning.[10] Emergency pacing in the management of hyperkalemia in a patient with associated digitalis and quinidine toxicity is reported here. Artificial pacing proved effective at a low excitation threshold. The heart remained contractile and responsive to extrinsic stimulation after intrinsic pacemakers failed.

Report of a Case

A 58-year-old woman with rheumatic heart disease, mitral valve prosthesis, chronic cardiac insufficiency and recurrent atrial fibrillation (Figure 1 A) was admitted to hospital for elective cardioversion. Additional diagnoses included diabetes, osteoarthritis, emphysema and chronic obstructive uropathy resulting from a lacerated left ureter.

On physical examination, the patient appeared chronically ill. A II/VI apical systolic murmur, metallic third heart sound, wheezes in both lungs, tender liver, pedal edema and Heberden's nodes were noted. Mild cardiomegaly, pulmonary congestion and interstitial fibrosis were seen on x-ray studies of the chest. Laboratory studies showed the following values: serum potassium, 5.4 mEq per liter; digoxin, 1.4 ng per ml; urea nitrogen, 17 mg per 100 ml, and prothrombin activity 40 percent.

Digoxin, 0.25 mg; furosemide, 80 mg; potassium chloride, 6 grams; potassium iodide, 1.6 gram; phenformin, 100 mg; oxytriphylline, 600 mg; indomethacin, 75 mg, and quinine, 1,000 mg were administered daily and the patient's warfarin dosage was increased for optimal anticoagulation. On the second day a misunderstanding led to a one-fold increase in the quinine dose for leg cramps; on the fifth and sixth days, 900 mg and then 1,200 mg of quinidine gluconate were given in anticipation of electrical cardioversion.

Next day the patient gradually became comatose, hypotensive, anuric and then moribund without benefit from intravenous atropine and isoproterenol therapy. Blood was drawn for determination of quinidine, digoxin, electrolyte and urea nitrogen levels. Findings on electrocardiograms (Figure 1 B-G) deteriorated throughout the day to a "sine wave" pattern which persisted for approximately an hour before a transvenous pacing electrode was inserted. Effective ventricular pacing was achieved immediately at a threshold of 0.5 milliampere (Figure 1 H). The blood pressure rose quickly to 110/70 mm of mercury, the patient became responsive within 30 minutes and a normal urine output resumed. An hour after pacing, a serum potassium level of 8.5 mEq per liter and urea nitrogen level of 36 mg per 100 ml were reported and the patient was treated with calcium chloride, 4 grams; sodium bicarbonate, 80 mEq; glucose, 50 grams, and insulin, 25 units given intravenously plus sodium polystyrene sulfonate (Kayexelate®), 100 grams given by retention enema. The electrocardiogram improved pro-

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gressively throughout the night with the pacemaker switched off at intervals (Figure 1 I-K); the patient recovered uneventfully, electrical cardioversion was carried out before discharge (Figure 1 L) and she remains alive two years later. The serum digoxin level was 3.4 ng per ml and the quinidine level 8.3 mg per liter at the height of cardiac dysfunction. Creatinine clearance measured six weeks after discharge was 26 ml per minute.

Discussion

A diagnostic puzzle confronted the staff the day this patient almost died. There was little to suggest potassium intoxication by the clinical presentation and initial tests of serum potassium and blood urea nitrogen. Tall sharp T waves commonly associated with mild hyperkalemia electrocardiographically were never seen. Characteristic tall, narrow and pointed T waves may be present, however, in only a fourth of patients with hyperkalemia.[1] With progressive bradycardia and widening of QRS complexes, it was realized the patient had received sizable doses of quinidine and quinine concurrently and an additive effect of these drugs was appreciated. Thus at the time of emergency cardiac pacing, quinine-quinidine* toxicity was the presumptive diagnosis. Hyperkalemia was not discovered and treated chemically until an hour after successful pacing had been achieved and the patient's condition had improved to a pronounced degree.

In retrospect, hyperkalemia was probably the dominant toxic factor resulting from overly-zealous potassium chloride supplementation and potassium iodide therapy in the presence of impaired renal function and from decreased renal plasma flow associated with heart failure and diuretic-induced hypovolemia. Surawicz and associates[12] reported a similar but fatal case of hyperkalemia in an elderly patient in whom heart failure was treated with sodium meralluride and 6 grams of potassium chloride daily for five days in the hospital. Indeed, the same renal and prerenal circula-

*The quinidine assay performed by Bio-Science Laboratories, Van Nuys, California is not specific, detects quinine, and the two are summated in the final quantitative result.

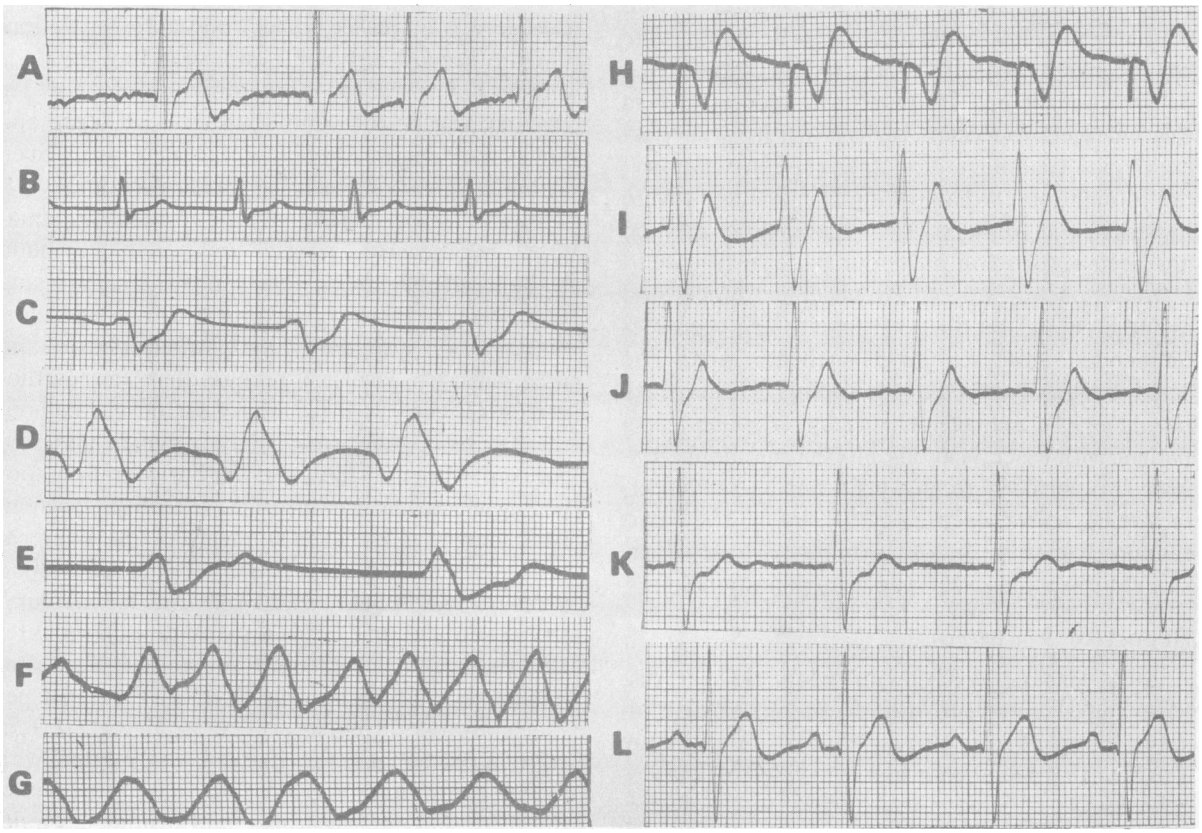

Figure 1.—The electrocardiographic sequence of cardiac arrest, artificial pacing and recovery from hyperkalemia, digitalis and quinidine toxicity. **A**, atrial fibrillation. **B**, sinoventricular or accelerated junctional (nodal) rhythm. **C, D, E**, sinoventricular or idioventricular rhythm. **F, G**, dying heart pattern. **H**, ventricular pacing. **I, J, K**, sinoventricular or accelerated junctional (nodal) rhythm. **L**, sinus rhythm.

tory disorders contributing to hyperkalemia probably led to an accumulation of quinine-quinidine and digoxin to plasma levels associated with toxicity at the time of circulatory collapse. It is well known that digoxin[13] and quinidine[14] reach higher plasma levels in patients with advanced heart disease and renal insufficiency compared with healthy subjects given comparable doses. Serum levels of digoxin in excess of 2 ng per ml[15] and quinidine in excess of 8 mg per liter[16] are commonly associated with toxicity.

Acute electro-mechanical heart failure was probably caused by a summation of potassium, quinine-quinidine and digitalis intoxication. First, the profound depression of cardiac automaticity and contractility was disproportionate to the moderate hyperkalemia measured (8.5 mEq per liter). Ventricular asytole is usually associated with plasma potassium levels above 12 mEq per liter. The extensive experience of Surawicz and associates with potassium infusions to control arrhythmias in man indicate that plasma potassium concentrations may be raised to 7 or 8 mEq per liter, temporarily at least, with no significant risk of cardiac arrest.[12] In the canine studies of Lee and co-workers[17] and Ham and co-workers,[18] ventricular stimulation thresholds have been shown to *decrease* with rising potassium concentrations up to 6.7 to 8.5 mEq per liter. Further elevations were associated with increasing excitation thresholds. Second, manifestations of quinidine toxicity include central nervous system disturbances,[10] depression of heart rate and contractility and progressive QRS widening[19] not unlike those changes observed in the patient reported here. Third, sinoatrial arrest and cardiac standstill may result from digitalis toxicity. At least one such case has been treated successfully by artificial pacing.[9] Complex interrelations exist between potassium, digitalis and quinidine, especially in patients with impaired renal function.[20,21] Digitalis may elevate plasma potassium levels in humans and provoke hyperkalemia, according to Mason and associates.[8] Decreased cardiac membrane potentials and speed of contraction induced by quinidine are accentuated by hyperkalemia[20] and the additive effects of hyperkalemia and quinidine therapy may depress myocardial contractility and result in serious toxicity.[21] Therefore, a combination of hyperkalemia, quinidine and digitalis toxicity provides the best explanation for the severity of the arrhythmias and circulatory failure in this patient when serum concentrations of potassium, quinidine and digoxin were elevated only moderately into the toxic range.

A low pacing threshold of 0.5 milliampere at the height of cardiac dysfunction was unexpected. Furman and associates[5,6] did not provide excitation thresholds in their reports of four hyperkalemic patients treated successfully by cardiac pacing. A fatal case described by Surawicz and associates[12] was refractory to pacing during an hour of cardiac arrest, then responded after treatment with adrenalin and sodium bicarbonate. The preterminal threshold was not reported. Subsequently these investigators observed increased pacing thresholds in six dogs and one human volunteer during intravenous infusions of potassium, 4- to 12-fold above preinfusion levels, but in no instance did they exceed 6 volts. Of greater interest, a top plasma potassium level above which pacing was ineffective was never reached. Potassium concentrations rose to 12, 13 and 15 mEq per liter in three dogs at which time pacing thresholds equalled only 2.9, 4.6 and 4.2 volts, respectively.

The hyperkalemic range within which life-threatening arrhythmias may occur and pacing refractoriness develops may be rather wide. The experiments of Surawicz and his co-workers[12] and the results obtained in the present case invite the exploration of the range of pacing thresholds at various levels of hyperkalemia in which the heart fails to contact spontaneously but remains responsive to artificial stimulation.

Summary

This report describes a 58-year-old woman with advanced rheumatic heart disease in whom profound electro-mechanical heart failure was treated successfully by emergency pacing. The cause for the near-fatal complication was obscure at the time of artificial pacing but hyperkalemia combined with digitalis and quinidine toxicity emerged as the cause from laboratory tests and a review of treatment and clinical course. Pacing proved effective at a low excitation threshold and the heart remained contractile and responsive after intrinsic pacemakers had failed. It is not widely known that cardiac pacing can be employed successfully in such an emergency.

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Bronchiolo-Alveolar Carcinoma Presenting as Pericardial Effusion with Tamponade

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WE WISH TO DRAW ATTENTION to several occurrences of large, life-threatening pericardial effusion which have turned out to be the first major clinical manifestation of unsuspected or undiagnosed lung cancer, particularly the type referred to as bronchiolar adenocarcinoma. Three case summaries, with autopsy findings, are presented.*

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Reports of Cases

CASE 1. A 55-year-old Caucasian man, a smoker, presented with a six-week history of exertional dyspnea, worsening of a chronic cough and increase in severity of chronic intermittent back and chest pain. On admission he was noted to become dyspneic on walking more than a few steps. The patient was in moderate distress with dyspnea, cough, back and lower chest pain. The neck veins were engorged. An increased anteroposterior chest diameter was noted as were a prolonged expiratory phase and diffuse rhonchi. The working diagnosis was chronic obstructive pulmonary disease with acute exacerbation of chronic bronchitis and severe myalgia secondary to cough.

Cardiomegaly and left upper and lower lobe infiltrates were seen on x-rays of the chest. On the seventh hospital day, tachycardia, tachypnea, cyanosis and pallor developed. The systolic pressure dropped to a pronounced degree, with a narrow pulse pressure. Shortly thereafter the patient died. Clinical impression of the cause of death was pneumonia due to chronic obstructive pulmonary disease.

At autopsy pleural fluid was noted bilaterally. The right lung weighed approximately 1,000 grams and there was a deep stellate central retraction on the anterior surface of the upper lobe. Microscopic sections through this area showed partially papillary adenocarcinoma, consistent with bronchiolar type, lining and permeating the crevices of an old hyalinized, partially-cavitated scar and extending into adjacent alveoli. The